REMARKS/ARGUMENTS

Support for new claims 103 and 104 is provided at, *e.g.*, p. 14, lines 19-20. Applicant uses the paragraph numbering of the office action in responding to the Examiner's remarks. Lack of comment on any of the Examiner's remarks should not be construed as acquiescence therewith.

¶7. Claims 82-90 and 93-102 stand rejected on the basis that the specification is allegedly not enabling for prophylaxis of disease, as claimed. The rejection is based in part on an alleged lack of working examples showing complete elimination of risk of disease. The Examiner also alleges that the PDAPP mouse model does not realistically reflect physiology in a normal asymptomatic subject. The Examiner further alleges that it would not be desirable to decrease levels of Aβ in a normal subject based on alleged teaching of Liu that Aβ has an important physiological role in normal mammals and on alleged teaching of Perez that the precursor of Aβ has such a role.

In reply, the PDAPP mouse referred to in the specification can be (and was) used as a model of both prophylaxis and therapeutic administration depending on the age of mice at which treatment is administered. Deposits do not start forming in such mice until the mice reach about 6 months old (*see* specification at p. 36, last paragraph). Thus, administration of agents before this age exemplifies prophylactic treatment, and administration of agents after this age exemplifies therapeutic treatment. The specification includes examples of both prophylactic and therapeutic treatment. For example, the experiment described at p. 36 of the specification is performed on mice at three months of age and that at p. 70 in the specification is performed on mice of 8.5-10.5 months of age. These and other examples in the specification show that antibodies can be effective both to inhibit formation of Aβ deposits before they have formed and to reduce such deposits after they have formed. It can be concluded from these experiments that administration of antibodies to Aβ, as claimed, has a pharmacological activity relevant to both prophylaxis and treatment of diseases characterized by deposits of Aβ.

The office action also intimates that the efficacy to side effects ratio is less favorable for prophylaxis than treatment. Even if this is true, it is submitted to be an issue for the patient, the treating physician and the FDA rather than the Patent Office. Few approved drugs are entirely free of side effects. The requirements under the law for obtaining a patent are not as stringent as the requirements for obtaining government approval to market a particular drug for human consumption. *In re Brana*, 34 USPQ2d 1436, 1442 (Fed. Cir. 1995). "Testing for full safety and effectiveness...is more properly left to the Food and Drug Administration (FDA). Title 35 does not demand that such human testing occur within the confines of Patent and Trademark Office (PTO) proceedings." *Id.* Emphasis added.

Applicant further notes that the Examiner's allegation that Aβ has an essential role in cellular physiology is not supported by the cited Liu reference. Liu proposes that alteration of vesicle transport by Aβ may be relevant to the chronic neurodegeneration of Alzheimer's disease (*see* abstract) but does not propose a role of Aβ in normal cellular physiology. With respect to possible depletion of APP, it is noted that six months of administration of various antibodies as described in Example XI had virtually no effect on APP levels (specification at paragraph bridging pp. 77-78). Thus, the Examiner's proposal that long term administration of antibodies to Aβ would have significant effect via depletion of APP is highly speculative.

Applicant has addressed the Examiner's comments regarding alleged lack of working examples illustrating elimination of all risk in the previous response. Applicant notes from the Examiner's comment in the penultimate sentence of the rejection that the Examiner may not be going so far as to allege that this alone would provide grounds for nonenablement. Thus, applicant does not further comment on this issue at this time.

¶¶8-10. The claims stand provisionally rejected for obviousness type double patenting over several US Patents. Applicant proposes the issues be held in abeyance until indication of allowability in the present case. Applicant maintains their offer to submit a terminal disclaimer over the cited patents if the claims are allowed in their current form.

¶11. Claims 1, 2, 4, 6-8, 10-12, 17, 21-24, 31-32, 35-37, 82-90, and 93-102 stand provisionally rejected for obviousness type double patenting over claims 56-195 of co-pending Application No. 10/828,548. Applicant respectfully points out that claims 56-176 and 178-195 of Application No. 10/828,548 have been canceled. Thus, the rejection is moot as to claims 56-176 and 178-195. Applicant proposes the issues be held in abeyance until indication of allowability in the present case. Applicant will then consider providing a terminal disclaimer over cited case provided the cited case has been or is about to patented, the claims in the cited case have not been divided from those in the present case by restriction requirement or election of species, and the claims in the cited case are in conflict with those in the present case at this time.

¶12. Claims 1, 2, 4, 6-8, 10-12, 17, 21-24, 31-32, 35-37, 82-90, and 93-102 stand provisionally rejected for obviousness type double patenting over claims 133-136 of co-pending Application No. 10/232,030. Applicant respectfully points out that claims 133-136 of Application No. 10/232,030 have been canceled. Thus, the rejection is moot and Applicant requests it be withdrawn.

¶13. Claims 1, 2, 4, 6-8, 10-12, 17, 21-24, 31-32, 35-37, 82-90, and 93-102 stand provisionally rejected for obviousness type double patenting over claims 1-52, 54-94, and 138-163 of co-pending Application No. 10/923,469. Applicant respectfully points out that claims 1-52, 54-94, and 138-163 of co-pending Application No. 10/923,469 have been canceled. Thus, the rejection is moot and Applicant requests it be withdrawn.

¶14. Claims 1, 2, 4, 6-8, 10-12, 17, 21-24, 31-32, 35-37, 82-90, and 93-102 stand provisionally rejected for obviousness type double patenting over claims 1-46 Application No. 10/890,071. Applicant respectfully points out that Application No. 10/890,071 has been abandoned (*see* Notice of Abandonment mailed July 13, 2007). Thus, the rejection is moot and Applicant requests it be withdrawn.

¶15. Claims 1-2, 4, 10-12, 22-23, 31-32 and 36 stand rejected as allegedly obvious over Becker in view of Kuby and Adair. Becker is alleged to teach treatment of Alzheimer's disease with antibodies to Aβ, Kuby is alleged to teach different isotypes of human antibodies, and Adair is alleged to teach that antibodies of human IgG1 isotype bind ICAM-1 more strongly than other isotypes. The Examiner alleges that it would have been obvious to use humanized antibodies of the IgG1 isotype in Becker's methods in view of Adair's teaching that IgG1 antibodies bind to antigens very well and Kuby's teaching that the properties of specific isotypes depend on the structure of the constant region not the variable region.

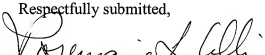
The Examiner's apparent inference from Adair and Kuby that human IgG1 antibodies generally have higher affinities than other isotypes is incorrect. Although Kuby indicates that certain properties of antibodies, such as complement activation, Fc receptor binding and ability to cross the placenta depend on isotype, he says nothing about binding affinity depending on isotype. Although Adair did report differences in binding affinity for different isotypes of the same antibody binding to ICAM-1, he states that this result was "unexpected because all these antibodies have identical binding sites" (p. 50, second paragraph), thus reflecting conventional wisdom that antibody binding is effected by the binding site rather than the constant regions (*see, e.g.*, Harlow & Lane, Antibodies: A Laboratory Manual at p. 23, second paragraph (1988), a copy of which is submitted herewith). Consistent with this view others have reported that binding affinity does not depend on isotype (*see* Boel et al., *J. Immunol. Methods* 239:153-166 (2000) at p. 161 and Preston, *Infection and Immunity* 66:4137-4142 (1998) at p. 4139, column 2, copies of both of which are submitted herewith.) Absent any evidence that higher affinity of human IgG1 was a general occurrence rather than an unexpected phenomenon for a particular antibody to ICAM-1, the skilled person would not have found Adair's result relevant to selection of isotype for the presently claimed methods.

For these reasons, it is respectfully submitted that the rejection should be withdrawn.

¶¶16-25. All of the remaining art rejections are also premised on the allegation that the combination of Kuby and Adair would have rendered obvious the selection of a human IgG1 isotype in the claimed methods. The distinctions discussed above are thus equally applicable.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-326-2400.

Respectfully submitted,



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